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Term: L4 same CETP

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L5	L4 same CETP	6	L5
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L5: Entry 1 of 6 File: PGPB May 29, 2003

DOCUMENT-IDENTIFIER: US 20030100520 A1
TITLE: IMMUNOLOGICAL PROCESS AND CONSTRUCTS FOR INCREASING THE HDL CHOLESTEROL CONCENTRATION BY DNA VACCINATION

Summary of Invention Paragraph:
[0029] The invention described hereinafter provides an autogeneic immunological process for the production of antibodies to CETP and can provide long-term lessening of transfer of cholesteryl esters from HDL particles in mammals whose blood contains CETP by utilization of a DNA vaccine. This process permits the long-term elevation of anti-atherogenic HDL cholesterol concentrations.

Summary of Invention Paragraph:
[0109] A variety of plasmids can be used as DNA vaccine vectors for expressing a contemplated CETP immunogen in a mammalian host. Such vectors optimally include the following components: a strong eukaryotic promoter, a cloning site for insertion of a gene of interest, a polyadenylation termination [poly(A)] sequence, a prokaryotic origin of replication, and a prokaryotic selectable marker. One such vector, pV1J, contains the cytomegalovirus immediate-early promoter with intron A, a bovine growth hormone polyadenylation termination sequence, and an ampicillin resistance gene. [J. B. Ulmer et al., ASM News, 62(9): 476-479 (1996).] Another useful vector denominated pcDNAI/Amp that is available from Invitrogen, Corp. of San Diego, Calif., as well as plasmids pCMV-SPORT-.beta.-gal and pGreen Lantern-1 available from Life Technologies, Rockville, Md. are discussed in detail hereinafter. Other eukaryotic promoters, poly(A) sites, and selectable markers can be substituted without departing from the utility of the vector, as long as the structural gene inserted downstream from the promoter is expressed in mammalian cells. A variety of general mammalian expression vectors, many of which are commercially available, are suitable for use herein as DNA vaccine vectors.

Summary of Invention Paragraph:
[0117] A DNA vaccine vector encoding a CETP immunogen in proper reading frame (a recombinant DNA molecule) and containing a promoter sequence that controls expression of the immunogenic polypeptide is dissolved or dispersed in a pharmaceutically-acceptable vehicle composition that is preferably aqueous to form an inoculum that when used to immunize a mammal induces the production of antibodies that immunoreact with (bind to) CETP. When that recombinant DNA molecule is administered in an effective amount to a mammal whose blood contains CETP those antibodies preferably also lessen the transfer of cholesteryl esters from HDL particles.

Detail Description Paragraph:
Construction of DNA Vaccine Vectors Capable of In Vivo Expression of HBcAg/CETP/HBcAg Fusion Proteins

Detail Description Paragraph:
[0206] D. Insertion of the Rabbit CETP gene into DNA Vaccine Vectors

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L3: Entry 1 of 9 File: PGPB Jun 12, 2003

DOCUMENT-IDENTIFIER: US 20030108559 A1
TITLE: Modulation of cholesteryl ester transfer protein (CETP) activity

Detail Description Paragraph:
[0072] An example of a recombinant plasmid that can be used to produce a vaccine peptide is plasmid pCMV-CETP/TT in which the CMV promoter directs transcription of a sequence encoding a vaccine peptide having the amino acid sequence of SEQ ID NO: 9: M Q Y I K A N S K F I G I T E R F P R P D G R E A V A Y R F E E D I F G F P K H L L V D F L Q S L S ,

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L3: Entry 4 of 9 File: USPT Apr 29, 2003

US-PAT-NO: 6555113
DOCUMENT-IDENTIFIER: US 6555113 B1

TITLE: Modulation of cholesteryl ester transfer protein (CETP) activity

DATE-ISSUED: April 29, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Rittershaus; Charles W.	Malden	MA		
Thomas; Lawrence J.	Worcester	MA		

US-CL-CURRENT: 424/193.1; 424/146.1, 424/185.1

CLAIMS:

What is claimed is:

1. A method of elevating the ratio of circulating HDL to circulating LDL, VLDL, or total cholesterol in a human or other animal comprising administering to the human or animal a vaccine composition comprising a peptide conjugate comprising a helper T cell epitope portion linked to a B cell epitope portion, wherein said B cell epitope portion comprises a B cell epitope of a CETP of a human or other animal, and said peptide conjugate, when administered to said human or other animal, elicits production of endogenous antibodies that specifically bind endogenous CETP and results in an elevation of the ratio of circulating HDL to circulating LDL, VLDL, or total cholesterol in said human or other animal.

2. A method according to claim 1 wherein said B cell epitope portion comprises between six and 26 consecutive amino acids of the carboxyl terminal 26 amino acids of human CETP (SEQ ID NO:1).

3. The method according to claim 1 wherein the helper T cell epitope portion of the peptide conjugate comprises a T cell epitope selected from the group consisting of the amino acid sequence of amino acids 830 to 843 of tetanus toxin protein (amino acids 2 to 16 of SEQ ID NO:2) and the amino acid sequence of amino acids 947 to 967 of tetanus toxin protein of SEQ ID NO:3.

4. The method according to claim 1 wherein the B cell epitope portion of the peptide conjugate is selected from the group consisting of between six and 26 consecutive amino acids of SEQ ID NO:1.

5. The method according to claim 1 wherein the peptide conjugate further comprises an amino terminal cysteine residue.

6. A method of decreasing the level of endogenous CETP activity in a human or other animal comprising administering to the human or animal a peptide conjugate comprising a helper T cell epitope portion linked to a B cell epitope portion comprising a B cell epitope of a CETP of a human or animal, wherein said peptide conjugate, when administered to said human or animal, elicits production of endogenous antibodies that specifically bind endogenous CETP and results in a decrease in the level of endogenous CETP activity in said human or animal.

7. The method according to claim 6 wherein the peptide conjugate is administered in an amount sufficient to elicit production in said human or other animal of anti-CETP antibodies.

8. A method of altering the catabolism of HDL-cholesterol to decrease the development of atherosclerotic lesions in a human or other animal comprising administering to the human or animal a peptide conjugate comprising a helper T cell epitope portion linked to a B cell epitope portion, said helper T cell epitope portion comprising a broad range T cell epitope and said B cell epitope portion comprising a B cell epitope of CETP, wherein said peptide conjugate, when administered to said human or animal, elicits production of endogenous antibodies that specifically bind endogenous CETP and results in a decrease in the development of atherosclerotic lesions in said human or animal compared to a human or animal not receiving such treatment.

9. A method of increasing the level of circulating HDL in a human or other animal comprising administering to the human or animal a peptide conjugate comprising a helper T cell epitope portion and a B cell epitope portion, wherein said B cell epitope portion comprises a B cell epitope of a CETP of a human or other animal, and wherein said peptide conjugate, when administered to said human or animal, elicits production of endogenous antibodies that specifically bind endogenous CETP and results in an increase in the level of circulating HDL in said human or animal.

10. The method according to claim 9, wherein the helper T cell epitope portion comprises a helper T cell epitope derived from an antigenic peptide selected from the group consisting of tetanus toxoid, diphtheria toxoid, pertussis vaccine, Bacile Calmette-Guerin (BCG), polio vaccine, measles vaccine, mumps vaccine, rubella vaccine, purified protein derivative of tuberculin, keyhole limpet hemocyanin, and combinations thereof.

11. The method according to claim 9, wherein the B cell epitope portion comprises a carboxyl terminal region of human CETP consisting of between six and 26 consecutive amino acids of SEQ ID NO:1.

L3: Entry 5 of 9 File: USPT Sep 4, 2001

US-PAT-NO: 6284533
DOCUMENT-IDENTIFIER: US 6284533 B1

TITLE: Plasmid-based vaccine for treating atherosclerosis

DATE-ISSUED: September 4, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Thomas; Lawrence J.	Easton	MA		

US-CL-CURRENT: 435/320.1; 435/455, 435/69.1, 514/44, 536/23.1, 536/23.4, 536/23.5

CLAIMS:

What is claimed is:

1. A DNA immunogenic composition comprising a nucleotide sequence coding for an immunogenic polypeptide, which nucleotide sequence includes at least one segment coding for a B cell epitope of cholesteryl ester transfer protein (CETP) linked in-frame with at least one segment coding for a broad range helper T cell epitope, which nucleotide sequence is operably linked to a promoter sequence suitable for directing the transcription of the nucleotide sequence in a mammalian cell.

2. The DNA immunogenic composition according to claim 1 wherein said at least one segment coding for a B cell epitope of CETP encodes a B cell epitope of human CETP and consists of 5-8 consecutive amino acids of SEQ ID NO:4.

3. The DNA immunogenic composition according to claim 1 wherein said B cell epitope comprises a carboxyl terminal region of CETP, involved in neutral lipid binding or neutral lipid transfer activity.

4. The DNA immunogenic composition according to claim 1 wherein the helper T cell epitope comprises a helper T cell epitope obtained from an antigenic peptide selected from the group consisting of tetanus toxoid, diphtheria toxin, pertussis vaccine, Bacile Calmette-Guerin (BCG), polio vaccine, measles vaccine, mumps vaccine, rubella vaccine, purified protein derivative of tuberculin, keyhole limpet hemocyanin, and combinations thereof.

5. The DNA immunogenic composition according to claim 1 wherein the immunogenic polypeptide includes two B cell epitopes of CETP.

6. The DNA immunogenic composition according to claim 5 which includes a DNA segment coding for amino acids 463 through 475 of SEQ ID NO: 4 and a DNA segment coding for amino acids 349 through 367 of SEQ ID NO: 4.

7. The DNA immunogenic composition according to claim 5 which includes a DNA segment coding for amino acids 461 through 476 of SEQ ID NO: 4 and a DNA segment coding for amino acids 349 through 367 of SEQ ID NO: 4.

8. The DNA immunogenic composition according to claim 1, wherein said at least one segment coding for a broad range helper T cell epitope encodes amino acids 2 through 15 of SEQ ID NO: 7.

9. The DNA immunogenic composition according to claim 1, wherein said nucleotide sequence coding for an immunogenic polypeptide encodes the amino acid sequence of SEQ ID NO:7.

10. The DNA immunogenic composition according to claim 1, wherein the promoter is a cytomegalovirus immediate early promoter/enhancer.

11. A DNA immunogenic composition comprising a nucleotide sequence comprising:

(a) an immediate early promoter/enhancer region of cytomegalovirus (CMV), operably linked to

(b) a structural DNA segment encoding an immunogenic polypeptide and comprising:

(i) a DNA segment encoding amino acids 2 through 15 of SEQ ID NO: 7,

(ii) a DNA segment encoding amino acids 463 through 475 of SEQ ID NO: 4, and

(iii) a DNA segment encoding amino acids 349 through 367 of SEQ ID NO: 4,

which DNA segments (i), (ii) and (iii) are linked in-frame.

12. A DNA immunogenic composition comprising a nucleotide sequence comprising:

(a) an immediate early promoter/enhancer region of cytomegalovirus (CMV), operably linked to

(b) a structural DNA segment encoding an immunogenic polypeptide and comprising:

(i) a DNA segment encoding amino acids 2 through 15 of SEQ ID NO: 7,

(ii) a DNA segment encoding amino acids 461 through 476 of SEQ ID NO: 4, and

(iii) a DNA segment encoding amino acids 349 through 367 of SEQ ID NO: 4,

which DNA segments (i), (ii) and (iii) are linked in-frame.

13. A DNA immunogenic composition comprising a nucleotide sequence coding for an immunogenic polypeptide, which nucleotide sequence comprises a first segment coding for a broad range helper T cell epitope linked in frame with a second segment coding for a first B cell epitope of cholesteryl ester transfer protein (CETP) having the nucleotide sequence of nucleotides 55 through 111 of SEQ ID NO:5 and a third segment coding for a second B cell epitope of CETP having the nucleotide sequence of nucleotides 112 through 159 of SEQ ID NO:5, wherein the

nucleotide sequence coding for the immunogenic polypeptide is operably linked to a promoter sequence suitable for directing the transcription of the nucleotide sequence in a mammalian cell.

14. The DNA immunogenic composition according to claim 13 wherein the nucleotide sequence comprises the nucleotide sequence of SEQ ID NO:5.

15. A DNA immunogenic composition comprising a nucleotide sequence coding for an immunogenic polypeptide, which nucleotide sequence comprises a first segment encoding a broad range helper T cell epitope linked in-frame with a second segment coding for a first B cell epitope of cholesteryl ester transfer protein (CETP) having the nucleotide sequence of nucleotides 1045 through 1101 of SEQ ID NO:3 and a third segment coding for a second B cell epitope of CETP having the nucleotide sequence of nucleotides 1387 through 1425 of SEQ ID NO:3, wherein the nucleotide sequence coding for the immunogenic polypeptide is operably linked to a promoter sequence suitable for directing the transcription of the nucleotide sequence in a mammalian cell.

16. A DNA immunogenic composition comprising a nucleotide sequence coding for an immunogenic polypeptide, which nucleotide sequence comprises a first segment coding for a broad range helper T cell epitope linked in-frame with a second segment coding for a first B cell epitope of cholesteryl ester transfer protein (CETP) having the nucleotide sequence of nucleotides 1045 through 1101 of SEQ ID NO:3 and a third segment coding for a second B cell epitope of CETP having the nucleotide sequence of nucleotides 1381 through 1428 of SEQ ID NO:3, wherein the nucleotide sequence coding for the immunogenic polypeptide is operably linked to a promoter sequence suitable for directing the transcription of the nucleotide sequence in a mammalian cell.

17. A DNA immunogenic composition comprising a nucleotide sequence coding for an immunogenic polypeptide, said nucleotide sequence being operably linked to a promoter sequence suitable for directing the transcription of said nucleotide sequence in a mammalian cell, said immunogenic polypeptide comprising a B cell epitope portion, wherein said B cell epitope portion comprises at least one B cell epitope of cholesteryl ester transfer protein (CETP), and a broad range helper T cell epitope portion, wherein said broad range helper T cell epitope portion comprises at least one broad range helper T cell epitope.

18. The DNA immunogenic composition according to claim 17, wherein said at least one B cell epitope of CETP consists of 5-26 consecutive amino acids of SEQ ID NO:4.

19. The DNA immunogenic composition according to claim 17, wherein said at least one broad range helper T cell epitope is a broad range helper T cell epitope obtained from an immunogenic peptide selected from the group consisting of tetanus toxoid, diphtheria toxin, pertussis vaccine, Bacile Calmette-Guerin (BCG), polio vaccine, measles vaccine, mumps vaccine, rubella vaccine, purified protein derivative of tuberculin, and combinations thereof.

20. The DNA immunogenic composition according to claim 17, wherein said immunogenic polypeptide includes two B cell epitopes of CETP.

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L5: Entry 1 of 6 File: PGPB May 29, 2003

PGPUB-DOCUMENT-NUMBER: 20030100520
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030100520 A1

TITLE: IMMUNOLOGICAL PROCESS AND CONSTRUCTS FOR INCREASING THE HDL CHOLESTEROL CONCENTRATION BY DNA VACCINATION

PUBLICATION-DATE: May 29, 2003

US-CL-CURRENT: 514/44; 536/23.2, 536/23.53

APPL-NO: 09/ 386591 [PALM]
DATE FILED: August 31, 1999
CONTINUED PROSECUTION APPLICATION: This is a publication of a continued prosecution application (CPA) filed under 37 CFR 1.53(d).

RELATED-US-APPL-DATA:
Application 09/386591 is a continuation-of US application 08/934367, filed September 19, 1997, PENDING
Application 08/934367 is a continuation-in-part-of US application 08/785997, filed January 21, 1997, PENDING
Application 08/934367 is a continuation-in-part-of US application 08/788882, filed January 21, 1997, PENDING

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This is a continuation-in-part of application Ser. Nos. 08/785,997 and 08/788,882, both filed Jan. 21, 1997.